platelet surface receptor changes is unknown. In addition, further clarification of the changes in hemostatic and rheological factors that can promote platelet aggregation and that may occur upon standing, are required.

Methods and Results: We therefore investigated the effect of arising in the morning on whole blood impedance aggregometry in 12 normal subjects and simultaneously measured platelet activation directly by using whole blood flow cytometry (n = 5). Aggregometry was completed and antibodies were added within 10 mins of blood withdrawal. Hemodynamic changes (n = 12), catecholamines (n = 6), fibrinogen (n = 6), platelet count and hematocrit (n = 8) were also measured. Platelet aggregation to ADP and collagen increased by 75% ($p < 0.01$) and 32% ($p < 0.01$) respectively. However, this was not associated with evidence of activation using flow cytometry. Six markers (GPIb, P-selectin, activated GPIIb-IIIa, GPIV, fibrinogen and vWF) tested with 10 antibodies showed no change in either percent positivity or flourescence intensity. Platelet count and fibrinogen levels increased by 14% ($p < 0.01$) and 12% ($p < 0.04$) respectively which was partly due to hemoconcentration (hematocrit increased by 7%, $p < 0.01$). Heart rate and norepinephrine levels significantly increased by 20% ($p < 0.02$) and 163% ($p < 0.01$) respectively.

Conclusions: The observed increase in whole blood platelet aggregation on arousal and standing in the morning is not accompanied by activation-dependent platelet surface receptor changes. Thus changes in rheological and hemostatic factors, such as increases in platelet count and fibrinogen level, together with indirect effects of increases in catecholamine levels may play a more important role in promoting platelet aggregation upon standing.

1013-112 Is the INR an Adequate Corrective Factor for the Range of Thromboplastins Utilized in North America?

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For a given intensity of anticoagulant therapy the Prothrombin Time Ratio (PTR) shows wide variability when measured with different thromboplastin reagents due to differing sensitivities of the commercially available thromboplastins as reflected in differences in the International Sensitivity Index (ISI) values for each reagent. The International Normalized Ratio (INR) is used to correct for this variation. We investigated the variability of INR obtained with 11 different thromboplastins from 4 different manufacturers using a single venipuncture sample from each of 49 unselected patients. The ISI values of the thromboplastins ranged from 1.0 to 2.81 and all analyses were performed on a MLA 700 instrument.

Results: For any individual thromboplastin the coefficient of variation (CV) was very low—1.6 to 4.6%. However, when comparing INR values from all 11 thromboplastins the CV was 19%, which was a significant improvement over the CV for PTR of 29%, ($p < 0.005$) but still high enough to allow for clinically significant differences as demonstrated by the following confidence ranges:

INR	95% Confidence Range		CV
	lower limit	upper limit	
1.6	1.2	2.0	13%
2.4	1.7	3.1	15%
3.7	2.0	5.3	23%
4.7	2.2	7.3	27%

The CV and the standard deviation were directly related to the INR with higher variability at higher levels of anticoagulant intensity.

Conclusion: While the INR offers a significant reduction in variance as compared to the PTR, it is suboptimal for the range of thromboplastins available in North America, and can result in clinically significant variation when comparing INR results between institutions utilizing different thromboplastins, especially at higher intensities of anticoagulation.

1013-113 Is Diabetic "Hyperadrenergic Orthostatic Hypotension" due to End Organ Resistance to Catecholamines?

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It has been previously reported that orthostatic hypotension occurs in some diabetics despite markedly increased standing plasma norepinephrine. The mechanism for this response remains unclear. We hypothesized that this "hyperadrenergic response" is triggered by accentuated postural venous translocation of blood volume (venous pooling). We assessed the hemodynamic (99m Tc-RBC) and catecholamine responses to upright posture in 54 diabetic patients (30 M: 24 F, age 57.5 ± 13 yrs). Venous translocation was defined by the ratio of cardiopulmonary volume (CPV) to total blood volume (TBV, RISA method). Total peripheral resistance was calculated from cardiac output and blood pressure. Based on upright plasma norepinephrine (UPNE), patients were classified as: hyperadrenergic if UPNE is >558 pg/ml, hypoadrenergic if UPNE <495 and normal adrenergic response if 494 >UPNE <558. Within each group, orthostatic hypotension OH+ was defined as a decrease in systolic blood pressure of >20 mmHg during tilt.

Results:

	HyperAdr		HypoAdr		Norm Adr	
	OH+	OH−	OH+	OH−	OH+	OH−
n	12	6	15	10	4	7
ΔSBP mmHg	−55±25	−12±6*	−53±23	−8±8*	−62±11	2±24*
ΔHR BPM	6±9	7±7	13±18	4±6	13±18	11±8
ΔTPR U.M^2	0.8±7	12±1.4	0.4±7	4±8	4±4	11±8
ΔCPV/TBV%	−2±1	−2.5±3	−1±3	−1±2	−2±1	−2±3
ΔP.NE Pg/ml	456±512	369±198	49±80†	98±65†	284±33	238±114

$\bar{x}$ ± SD *$p < 0.0001$ vs OH+ (HyperA, HypoA & Norm A), †$p < 0.01$ vs OH+ (HyperA). TPR = total peripheral resistance

Conclusions: Contrary to our hypothesis, orthostatic venous pooling was not accentuated in diabetics with hyperadrenergic OH+. Their disease is probably due to end organ resistance to plasma norepinephrine.

1013-114 Effect of Nitric Oxide on the Pulmonary Vascular Pressure-Flow Relationship in a Canine Model of Thrombolytic Pulmonary Hypertension

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Nitric oxide (NO) has been shown to be effective in reducing pulmonary artery pressure in many forms of pulmonary hypertension. While the intracellular mechanism of action is known, the pulmonary hemodynamic effects are not fully elucidated. This study examined the effects of inhaled NO on the pulmonary vascular pressure-flow (P-Q) relationship in a canine model of pulmonary embolism. According to P-Q theory, the slope of the P-Q plot defines the incremental vascular resistance (unit pressure change per unit change in flow) and the extrapolated pressure intercept defines the effective vascular outflow pressure. Six dogs were embolized with autologous blood clot to create pulmonary hypertension complicated by a low cardiac output state. To define the P-Q plot, multiple mean pulmonary artery pressure (PAP) vs cardiac output (CO) coordinates were obtained pre and post embolization, and before, during and after treatment with nitric oxide (180–200 ppm). The PAP-CO coordinates were obtained by varying flow through systemic arteriovenous fistulas. Embolization increased PAP (14.8 ± 1.2 to 34.6 ± 4.6; $p < 0.001$) and decreased CO (3.45 ± 0.63 to 2.25 ± 0.43; $p < 0.05$). All PAP-CO relationships were well described by a linear equation (mean r value 0.921 ± 0.029). Both the slope and intercept of the PAP-CO plot increased with embolization, (1.41 ± 0.09 to 3.51 ± 1.22; $p < 0.05$ and 9.9 ± 1.1 to 28.0 ± 6.5; $p < 0.005$ respectively). NO significantly improved pulmonary hemodynamics. The intercept of the PAP-CO plot decreased from the initial control of 28.0 mmHg to 22.5 mmHg ($p < 0.05$), and following discontinuation of the NO, increased to 26.2 mmHg ($p < 0.05$). The slope was not affected. Furthermore, NO did not affect systemic hemodynamics. In this model of pulmonary embolism, the increase in PAP is predominantly explained by an increase in the extrapolated pressure intercept (P_I) and NO selectively improved pulmonary hemodynamics by decreasing P_I. *Conclusion:* Based on previous work, it is most likely that the decrease in P_I represents a localized decrease in pulmonary vascular tone upstream from the capillary bed.

1013-115 Effect of Pravastatin on Abdominal Aorta and Carotid Wall Thickness in Dyslipidemia

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We studied 85 pts (45 female, 40 male, aged 55 ± 5 yrs) with familiar dyslipidemia, to assess the effect of pravastatin 15 mg daily orally administered on abdominal aorta (AA) and carotid (C) wall thickness (WT) compared to variation of total cholesterol (TCH) and LDL plasma levels. All underwent a 3 months period of dietary fat restriction and included in the study when TCH was still >240 mg/dl after this period. AA-WT and AA-WT corrected by the radius (AA-WT/r) were obtained using echography with a 3.5 MHz transducer, whereas C-WT and intima-media thickness (IMT) were obtained using a 5 MHz one. Media wall thickness (MWT = CWT − IMT) was also considered. Measurements were detected on basal and after 4.5 ± 1.2 months of therapy. The following results were obtained and compared by means of paired data t test: